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WHOLE-BODY VIBRATION EXERCISE IMPROVES FUNCTIONAL PARAMETERS IN PATIENTS WITH *OSTEOGENESIS IMPERFECTA*: A SYSTEMATIC REVIEW WITH A SUITABLE APPROACH

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## Abstract

**Background:** Patients with *osteogenesis imperfecta* (OI) have abnormal bone modelling and resorption. The bone tissue adaptation and responsivity to dynamic and mechanical loading may be of therapeutic use under controlled circumstances. Improvements due to the wholebody vibration (WBV) exercises have been reported in strength, motion, gait, balance, posture and bone density in several osteopenic individuals, as in post-menopausal women or children with disabling conditions, as patients with OI. The aim of this investigation was to systematically analyse the current available literature to determine the effect of WBV exercises on functional parameters of OI patients.

**Materials and methods:** Three reviewers independently accessed bibliographical databases. Searches were performed in the PubMed, Scopus, Science Direct and PEDro databases using keywords related to possible interventions (including WBV) used in the management of patients with *osteogenesis imperfecta*.

**Results:** Three eligible studies were identified by searches in the analysed databases.

**Conclusion:** It was concluded that WBV exercises could be an important option in the management of OI patients improving the mobility and functional parameters. However, further studies are necessary for establishing suitable protocols for these patients.

**Keywords:** whole body vibration exercise, *osteogenesis imperfecta*, mobility, functional parameters, Databases.

## Introduction

*Osteogenesis imperfecta* (OI), also known as brittle bone disease, is a rare and hereditary connective tissue disorder which occurs in approximately 1 in 15,000 to 25,000 of the population (Semler et al., 2008). It is a debilitating disorder with severe impact on functioning and quality of the life (QoL) (Engelbert et al., 2000). Subjects with OI present small body stature, hypotonia and joint hypermobility and, although no neurological deficits are present, experience developmental delays (Engelbert et al., 2000). Due to the frequent fractures and the periods of immobilization after surgery, individuals with OI are typically weaker than their age-matched peers (Biggin and Munns, 2014). The downward spiraling effect of immobilization resulting in decreased activity causes additional decrease in muscle and bone mass increasing their risk for low energy (non-traumatic) fractures (Rauch and Schoenau, 2001). The secondary complications are severe and include scoliosis (Sillence et al., 1979; Rauch and Glorieux, 2004) and other bone deformities (Engelbert et al., 2000b). Severely affected individuals have reduced mobility and often depend on a wheelchair (2). Infants with the worst form of OI are reported to die in the perinatal period (Biggin and Munns, 2014).

In 90% of cases, OI is related to the collagen Type-1 deficiency (Lindahl et al., 2015) and it is caused by dominant mutations in the collagen genes COL1A1/A2 or IFITM-5. Consequently, there is a quantitative or haploinsufficiency effect of col-1 production (Van Dijk et al., 2009). In about 15% of the cases, OI is inherited in a recessive manner due to mutations in genes that affect the bone modelling and resorption (Van Dijk et al., 2014). This process leads to strongly active bone remodelling, disorganized bone tissue, a reduction in trabecular and cortical bone mass and a decrease in bone mechanical properties (Semler et al., 2007). In the mild forms, OI may present premature osteoporosis or severe postmenopausal bone mineral loss (Engelbert et al., 2000; Van Dijk et al., 2009; Biggin and Munns, 2014).

There is no direct cure for OI. However, there are interventions that may provide symptomatic relief and reduce the risk of falling and fractures in these children (Van Dijk et al., 2014). The recommended approach includes medical and therapeutic intervention (Glorieux, 2016). Pharmacologic intervention with growth hormone therapy (Glorieux, 2016) and bisphosphonates (Sillence et al., 1979; Ward et al., 2004) to reduce the bone resorption has shown an

increase in bone mass and a reduction in fracture as well as pain (Rauch and Glorieux, 2004 and 2005). Regarding to the therapeutic intervention, there are recommendations as: (a) behavioral and lifestyle modifications, preventing fracture, (b) orthopaedic surgery, aiming to restore the bone deformation and biomechanical alignment (Semler et al., 2008), (c) scoliosis management, to minimize the column deformities (d) rehabilitation, including water therapy and physical activity, aiming to improve the quality of life (e) adaptive equipment and ambulation aids, to facilitate the daily activities and (f) weight management, to decrease the functional limitations (Glorieux, 2016). The less invasive physiotherapeutic approach is aimed at restoring function and reducing pain. Strengthening especially targeting the postural muscles, and exercise aimed at improving joint stability and electrotherapy for pain management are usually prescribed. The physical therapy is recommended for individuals with moderate/severe type of OI. When the OI is more severe, water therapy would be more appropriate (Thomas and DiMeglio, 2016). Children born with OI are given medication from an early age (2-5 years) and often for long periods at a time aiming to try to improve the impact on the growing skeleton (Van Dijk et al., 2014). The evidence for this effect on reducing the risk for fractures is however not clear (Castillo and Samson-Fang, 2009). The accumulation of those drugs and the impact thereof on bone remodelling over long periods results in highly mineralized bone of poor quality (Forlino et al., 2011). Bone tissue is widely responsive to dynamic loading and would be able to adapting response to the load (Rubin and Lanyon, 1985; Duncan and Turner, 1995; Judex and Zernicke, 2000; Ozcivici et al., 2010). It has been shown that a relationship exists muscle force and bone strength (Rauch and Schoenau et al., 2001). However, participation in regular sport activities is not an option for most children with OI due to their reduced exercise capacity and their increased fracture risk (Van Brussel et al., 2008). There is paucity in the literature regarding optimal or best practice exercise intervention programs for these children (Engelbert et al., 2000a). Following these considerations, Van Brussels et al., 2008 showed that a supervised training of exercises during 3 months can improve aerobic capacity and muscle force, and reduce the levels of subjective fatigue in children with OI type I and IV in a safe and effective manner.

Although WBV was initially developed to minimize the effects of weightlessness in astronauts in space (Rittweger et al., 2000; Blottner et al., 2006), authors have demonstrated that it can significantly increase strength with associated improvement in posture, gait and balance in various populations including the healthy sporting population (Tsuji et al., 2014). Studies using animal models (sheep, rat, and mouse) have shown that WBV can significantly affect bone formation (Flieger et al., 1998; Rubin et al., 2002a; Rubin et al., 2002b; Judex et al., 2002). This has been shown to occur across the ages (growing, young or old adults) (Xie et al., 2006 and 2008; Lynch et al., 2010). WBV exercise has increased bone density in several osteopenic individuals, such as in post-menopausal women (Verschueren et al., 2004; Roelants et al., 2004; Ruan et al., 2008; Mikhael et al., 2010) and children with disabling conditions such as with cerebral palsy (Ward et al., 2004; Sá-Caputo et al., 2015).

WBV exercise is generated when a subject is in contact with an oscillating/vibratory platform. These platforms produce mechanical vibration, and this physical agent is transmitted to the body of the subject generating WBV exercise (Rittweger et al., 2000; Tsuji et al., 2014; Rauch et al., 2010).

The therapeutic bases of the WBV exercise are related to the activation of proprioceptive spinal circuits (Semler et al., 2007). The rapid change in muscle length while standing on the platform vibrating at high frequency and low amplitude activates the stretch reflex facilitating a muscle contraction. When the person also voluntarily contracts together with the stimulus, the repetitive nature of the positioning and or movement is reinforced and strengthening occurs. This modality for exercise is increasingly being used also in the pediatric population to improve neuromuscular performance in children with various conditions and or disabilities (Ward et al., 2005; Semler et al., 2007; Rauch et al., 2010; Stark et al., 2010). Reports show that this kind of exercise is safe to use with no injuries been reported and very few side effects (Semler et al., 2007; Semler et al., 2008).

Although authors have described the effect of WBV exercises on bone mass in persons with OI (Semler et al., 2007; Semler et al., 2008; Hoyer-Kuhn et al., 2014), the basis of this finding is not clear yet. Studies have included patients with several types of OI, as: (i) types I, III, IV and V (41) and (ii) types III and IV (Semler et al., 2007; Semler et al., 2008). Sometimes, it is not possible that the patients of different clinical conditions be in a stand position on the base of the oscillating/vibratory platform. In this case adaptations are required (Menéndez et al., 2015; Pinto et al., 2011; Semler et al., 2007; Semler et al., 2008; Hoyer-Kuhn et al., 2014). Various studies utilised different parameters and a variety of results has been reported. Hoyer-Kuhn et al. 2014 included 6 months of WBV training in their 12 months of physiotherapeutic program in children with physical disabilities. This training included side alternating whole body vibration training, concomitant physiotherapy, resistance training and treadmill training. In the cohort of children with OI, improvements of motor function were observed in the group following the inclusion of WBV. But, the study was unable to conclude the effect of the additional WBV. The authors however recommended that WBV could be considered as additional therapeutic approach for children with severe OI. WBV exercise remains an attractive approach to stimulate bone formation in subjects with OI due to it has low impact and has the potential to improve motor performance or mobility and function in this population (Van Dijk et al., 2014).

The purpose of this review was to systematically analyse the current available literature to determine the effect of WBV on functional parameters of OI patients.

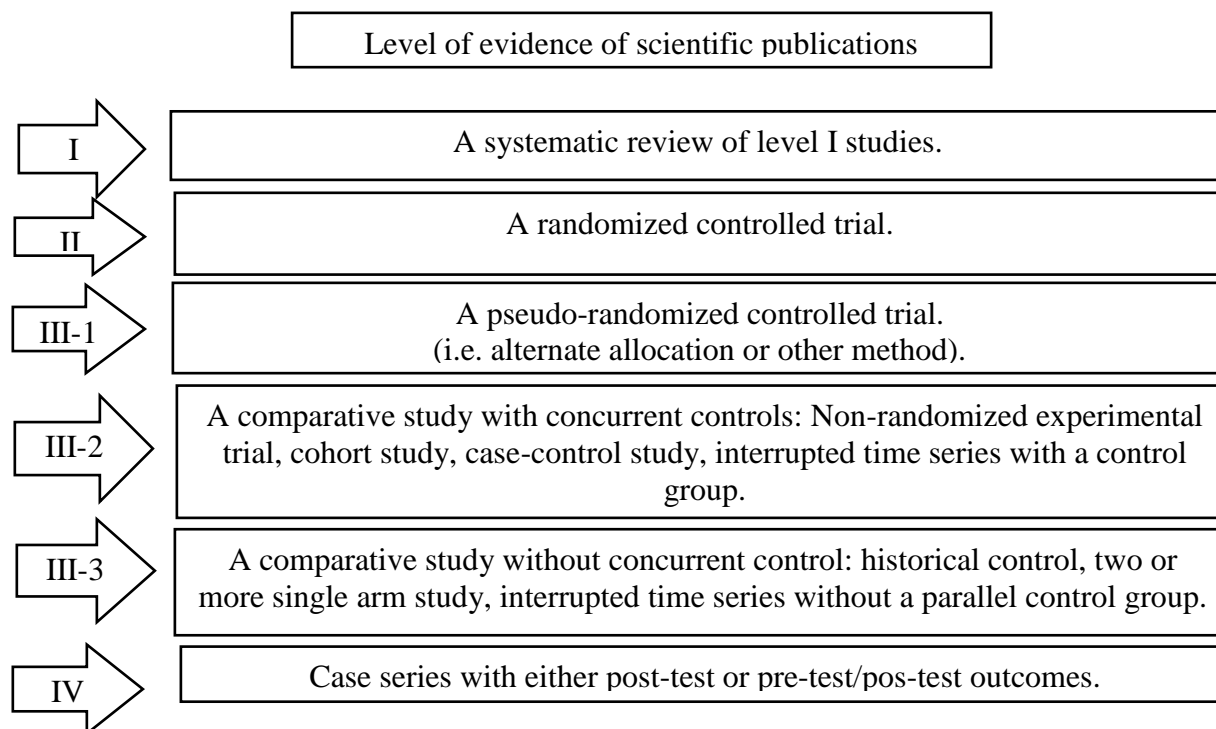
Three reviewers (D.S.C, E.M.M. and C.R.G.) independently accessed bibliographical databases through the Universidade do Estado do Rio de Janeiro. Searches were performed in the PubMed, Scopus, Science Direct and PEDro databases on August 3<sup>rd</sup>, 2015 using keywords related to possible interventions used in the management of OI patients. They were: (i) "*osteogenesis imperfecta*" or (ii) "*osteogenesis imperfecta*" and "whole body vibration", or (iii) "whole body vibration" or (iv) "*Osteogenesis imperfecta*" and "bisphosphonate" and or (v) "*osteogenesis imperfecta*" and "exercise". (Table 1).

**Table 1:** Number of publications in the PubMed, Scopus, Science Direct and PEDro databases.

Keywords	PubMed	Scopus	PEDro	Science Direct
" <i>osteogenesis imperfecta</i> "	4,703	6,371	1	6,677
" <i>osteogenesis imperfecta</i> " and "whole body vibration"	4	6	0	21
"whole body vibration"	1,323	2,636	184	2,254
" <i>osteogenesis imperfecta</i> " and "bisphosphonate"	189	276	0	41
" <i>osteogenesis imperfecta</i> " and "exercises"	26	63	1	706

### Eligibility Criteria

To be included in this review, the studies had to conform to the following variables: (i) Randomized controlled trial (RCT) or in the absence of RCT's, single group experimental studies were also considered (cross-over designs or case series), (ii) Studies had to investigate the effect of static or dynamic exercises while standing on an oscillating/vibratory platform in children, adolescents and/or adults with OI and (iii) Articles had to be published in the English language. Preliminary searches allowed for the elimination of unnecessary publication in each database. From appropriate sounding titles, abstracts were read and those that seemed to adhere to the inclusion criteria were downloaded and further reviewed, as it is shown in a flowchart. All the variables were put in separate tables and each reviewer indicated if the publication could be included in the current study. Regarding to each variable, the independent reviewers indicate yes or no. To be included in this study, the paper must have, at least, two yes. A flowchart following the PRISMA recommendations (Liberati et al., 2009) was done to show the steps in the selection of the full publications analyzed in this systematic revision (Figure 1).



**Figure 1:** Level of evidence of scientific publications, adapted from National Health and Medical Research Council (NHMRC-additional levels of evidence and grades for recommendations for developers of guidelines. Stage 2 consultation, Early 2008 – end June 2005).

### Exclusion criteria

The publications were excluded due to they were (a) not published in the English language, (b) a reply related to a question about a paper, (c) with healthy individuals, (d) with animal research, (e) with other techniques, (f) with occupational activities, (g) editorials or letters or abstracts, (h) about studies only with other diseases and (i) duplicates or triplicates.

### Level of evidence and methodological quality of the publications

Studies were rated according to their level of evidence (Figure 1) as described by National Health and Medical Research Council (NHMRC) hierarchy of evidence (NHMRC, 2013) and critically appraised using these criteria by each of the three reviewers. The rating and scores for each included study was cross-checked by a second reviewer and where there was disagreement a third party was consulted and the issue discussed until consensus was reached. Moreover, the methodological quality of these studies was determined by the PEDRo scale (PEDRo scale, 1999). In the PEDRo scale, each publication was evaluated according to: (a) eligibility criteria, (b) subjects were randomly allocated to groups, (c) concealed allocation, (d) the groups with baseline similarity, (e) blinding of the patients, (f) blinding of the therapists, (g) blinding of all assessors, (h) measures obtained from more than 85% of the subjects, (i) all subjects received the treatment or control condition or, at least one key outcome was analysed by “intention to treat”, (j) results of the groups with statistical comparisons and (h) point measures and measures of variability of outcome. Those publications with a score of seven or greater in the PEDro scale were considered of ‘high’ methodological quality, those with a score of five to six would be of ‘fair’ quality and a score of four or below were classified as ‘poor’ quality (Walser et al., 2009).

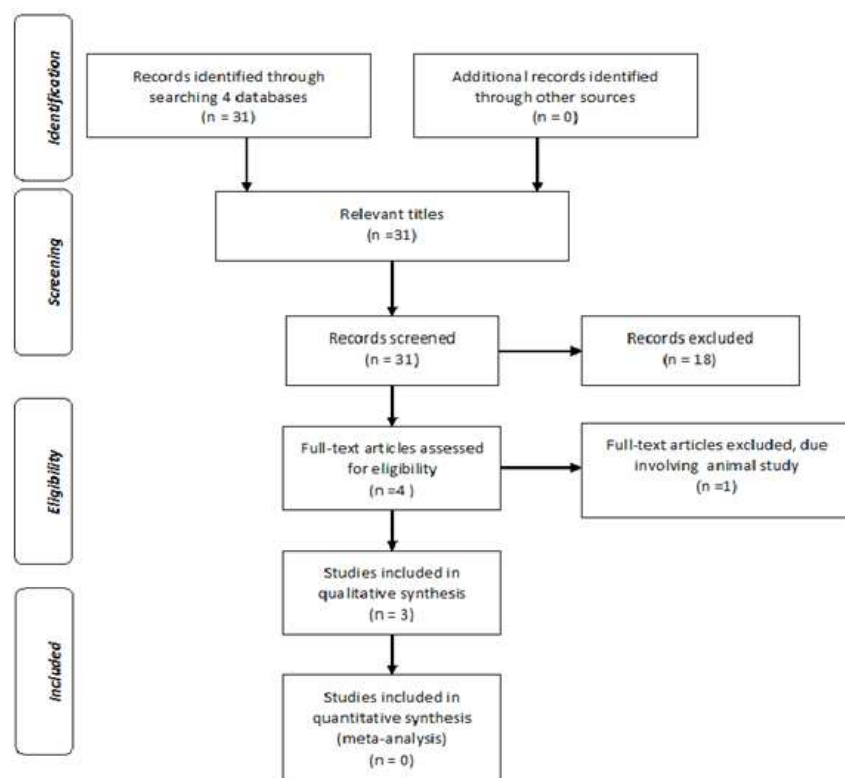
### Data extraction and processing

The selected papers were analysed and all the relevant data were extracted. Data were not comparable and therefore statistical pooling not appropriate with the result that the findings of this review are summarized in a narrative form.

## Results

Table 1 summarises the initial hits related to each keyword. It is shown that in three of the four databases searched have more than 4,700 publications involving OI. Considering some modalities of treatment of OI, in general, a small quantity of the publications involves the keyword “whole body vibration” in comparison with “exercise” or “bisphosphonate” independently on the databases searched.

Figure 2 presents a flow chart detailing data extraction procedures. The abstracts of 31 articles were screened and 18 were excluded due to they were (a) not published in the English language, (b) reply related to a question about a paper, (c) with healthy persons, (d) with animal research, (e) other techniques, (f) with occupational activities, (g) editorials or letters or abstracts, or (h) about studies only other diseases. Nine articles were duplicates (or even triplicates) which left three studies (Semler et al., 2007; Semler et al., 2008; Hoyer-Kuhn et al., 2014) to be included in the final review (Figure 2).



**Figure 2:** Flowchart indicating the steps to selected the full paper analyzed in this revision.

Table 2 shows the descriptions of the level of the evidence of the publications and the methodological quality assessment. The anthropometric characteristics of the participants, the aim, the protocol and the main outcomes and findings are also reported. Following the level of evidence (NHMRC, 2013), all the studies included in the current review (Semler et al., 2007; Semler et al., 2008; Hoyer-Kuhn et al., 2014) were considered III-3 classification. Following the PEDRo scale, all the studies (Semler et al., 2007; Semler et al., 2008; Hoyer-Kuhn et al., 2014) were considered of “poor” quality. All three studies used the same device namely Galileo® or Galileo TT®, Novotec Medical GmbH, Pforzheim, Germany, that is a side alternating (while the right foot is going down, the left foot is going up and vice versa) vibration platform. This equipment is supplemented by a tilt-table (Semler et al., 2007; Semler et al., 2008; Hoyer-Kuhn et al., 2014), and it possibility that patients with type serious of OI can be submitted on this treatment. The frequency varied from 15 to 25 Hz and the amplitude, from 0 (zero) up to 6 mm. Considering the importance of the peak to peak displacement (38), among the publications, Hoyer-Kuhn et al, 2014 described the peak acceleration of the vibration (3.53g to 15 Hz and 6.28g to 20 Hz), while this information is not found in the other papers (Semler et al., 2007; Semler et al., 2008). Sixty-seven individuals have participated in the studies with age from 4.9 up to 15 years old and 52.2% of them were male. Considering the aims of the investigations, different approaches are verified. All the papers present conclusions indicating the importance of the WBV to improve clinical condition of the patients with OI related to functional parameters. In general, different tools were used to evaluate the effect of WBV in patient with OI, although the “Brief Assessment of Motor Function” (BAMF) was used in all the studies. In addition, Hoyer-Kuhn et al, 2014 have also used the “Gross Motor Function Measure” (GMFM), the 1-minute walking distance (1min-WD), the areal bone mineral density (aBMD) and the Dual-energy X-ray absorptiometry (DXA) to determination of the lean mass. Moreover, only Hoyer-Kuhn et al, 2014 reported that the skidding was controlled by barefoot standing and manual fixation of the feet, if necessary. Considering the tilt table angle, (i) Semler et al, 2008 fixed it in 10 °, although, the angle of the knees could vary between 10 and 45 degrees during WBV training, (ii) Hoyer-Kuhn et al, 2014 altered it individually between 0-90 ° and (iii) Semler et al, 2007 altered it individually between 10-90 °. In all the studies the exposition to the WBV was 6 months and the additional therapies of the patients were maintained. Considering the findings reported in the Table 2, Hoyer-Kuhn, 2014 concluded that in a cohort study of OI children that participated in the specialized treatment with WBV, improvements of motor function were observed. It would be suggested WBV as additional therapeutic approach for children with severe OI. Semler et al., 2008, have also considered that WBV may be a promising approach to improve mobility in children and adolescents severely affected with OI. Semler et al., 2007, also concluded that WBV might be a promising approach to improve mobility in severely motor-impaired children and adolescents. Therefore, the CSWT powered by Galileo is a suitable therapeutic device to apply WBV in immobilized children and adolescents.



**Table 2:** Data about the level of evidence, the methodological quality, the number, sex and age of subjects, frequency, amplitude, aim, protocol and findings of the selected studies

Reference	LE and MQ	Number of subjects/sex/age	Frequency (Hz)	Amplitude (mm)	Aim	Protocol	Findings
Hoyer-Kuhn <i>et al.</i> , 2014	LE – III-3 MQ- Poor	53 children with OI (32 males and 21 females), 9.1±0.61 years	15-20	0 - ±3.9	To evaluate the effect of a side alternating WBV on motor function in children with OI	A training was performed in a SPRC and the baseline assessment (M0) was taken. After it, the children exercised (WBV) at home twice daily (each time 3x3 min) for 3 months. Afterwards they stay (6 consecutive days) took place in the SPRC. Therapy was adjusted to the progress of the child. Again, 3 months home-based WBV training followed. Six months after M0, the children were assessed (M6) and the WBV was returned to the clinic. After 6 further months (M12) another outpatient visit was performed to analyse motor function after 6 months follow up without WBV training.	A significant increase of motor function (GMFM-66 score 55.47±2.45 to 58.67±2.83) and walking distance (47.04±6.52 to 63.36±8.25 m) between M0 and M12 was seen. BAMF levels increased significantly from score 6.84±0.47 to 7.52±0.41. Total body without head bone mineral density increased significantly at M12.
Semler <i>et al.</i> , 2008	LE – III-3 MQ- Poor	8 patients with OI (3 males and 5 females), aging from 4.9 up to 14.9 years	15-25	1-2	To evaluate the effect of WBV on the mobility of long-term immobilized children and adolescents with a severe form of OI.	The therapeutic programme was conducted over a period of 6 months. Patients and their parents were instructed in the use of the CSWT System Galileo by a physiotherapist before the training equipment was installed at home. The programme comprised 2 daily therapy sessions with 3 cycles each. The tilting-angle and the frequency were adapted and increased in relation to the increase in the patient's physical ability. Tilting-angle and BAMF were measured at the start of WBV (M0), after 3 months (M3) and after 6 months (M6) of training	All individuals were characterized by improved muscle force documented by an increased tilting-angle (median=35 degrees) or by an increase in ground reaction force (median at start=30.0 [N/kg] (14.48–134.21); median after six months=146.0 [N/kg] (42.46–245.25). BAMF at M0 was significantly lower than at M3. Mobility scores were not different between M3 and M6.
Semler <i>et al.</i> , 2007	LE – III-3 MQ- Poor	6 long-term immobilized children with OI (6 females), aging from 5 up to 15 years	15-22	0-6	To verify effects of the CSWT powered by Galileo on the mobility of subjects with physical immobilization.	WBV was applied to 6 children and adolescents (OI, cerebral palsy, dysraphic defect of the lumbar spine) over a time period of 6 months. WBV was applied by a vibrating platform constructed on a tilt-table. The treatment effect was measured by alternations of the tilt-angle of the table and with the BAMF	All 6 individuals were characterized by an improved mobility, which was documented by an increased tilt-angle or an improved BAMF-score

LE- Level of Evidence, MQ- Methodological Quality, OI- Osteogenesis Imperfecta, WBV – Whole Body Vibration, CSWT- Cologne Standing-and-Walking-Trainer, M0- Baseline, M3- After 3 months with WBV training, M6- After 6 months of Training with WBV, M12- After 6 further months of follow up (without WBV), SPRC - Specialized Pediatric Rehabilitation Centre, BAMF - "Brief assessment of motor function", GMFM- Gross Motor Function Measure.

## Discussion

The relevance of the interventions as exercise and bisphosphonate is also shown in comparison with a possible alternative and safe procedure (WBV exercises) in patients with OI. WBV exercise has been used successfully in the management of other similar diseases with impairment of the motor functional, as cerebral palsy (Sá-Caputo et al., 2015), dysraphic defect of the lumbar spine (Semler et al., 2007), Duchenne muscular dystrophy (Söderpalm et al., 2013) and spinal cord injury (Menéndez et al., 2015).

Only a limited number of publications was found involving the use of WBV in OI patients and of the three publications that fulfilled the criteria to be considered in this study. All the publications were with a level of evidence of III-3 following the NHMRC. Moreover, all these publications were considered to have a “poor” methodological quality in the PEDRo scale. These findings suggest the need of additional research with a better methodological quality in this area.

Considering the conclusions of the papers analysed in this investigation, it is possible to consider that WBV exercise improves the functional parameters of OI patients, as increase of motor function (GMFM-66 score), walking distance and BAMF levels (motor function). Total body without head bone mineral density also increased.

The biomechanical parameters of the vibration used to generate WBV must be considered. The frequency used in the selected papers varied between 15 up to 25 Hz (Semler et al., 2007; Semler et al., 2008; Hoyer-Kuhn et al., 2014). This finding is in agreement with Sá-Caputo et al., 2015 that have presented in a review with WBV that were used frequencies between 5 and 25 Hz (50) and between 12 and 18 Hz (51) in the management of patients with cerebral palsy. In addition, Myers et al, 2014 have used frequencies from 7 to 20 Hz to treat patients with Duchenne muscular dystrophy. Concerning to the type of platform used in the selected studies, side alternating vibration platforms were used in all the investigations involving patient with OI (Table 2). The importance of this kind platform to produce suitable vibrations to be used in patient with disabilities, as presented by Lee and Chon, 2013 that have used it in the management of cerebral palsy patients. Considering patients with Duchenne muscular dystrophy, Myers et al., 2014 have also used side alternating vibration platform.

OI is a rare disorder (Semler et al., 2008) and in about 15% of the cases is related to the process of bone modelling and resorption (Van Dijk et al., 2014). In consequence, there is a decreased of the bone mechanical properties (Semler et al., 2007). Depending on the form of the OI can occur premature osteoporosis or severe postmenopausal bone mineral loss. In other form, patients can suffer multiple fractures with minimal or no trauma, and infants with the worst form of OI die in the perinatal period. These manifestations of OI lead to a reduced stability of the musculoskeletal system and to muscular hypotony in most patients (Rauch and Glorieux, 2004). Due to the effects associated with the use of WBV exercise, this modality the treatment would be very useful to the OI patient. Increase of the bone mineral density and improvement of the muscular strength (Semler et al., 2008; Rittweger et al., 2003) are some the effects of the WBV that can aid the OI patient. In addition, authors (Duncan and Turner, 1995; Ozcivici et al., 2010) have described that the bone tissue would be responsive to dynamic loading and it would be able to adaptation according to the mechanical loading, changing its structure. Some factors would be relevant in this context and these interfere in bone remodelling process. Rittweger et al., 2003 have pointed out that lower frequencies decrease the muscular tonus in contrast to higher frequencies, which increase the muscular tonus. It is considered that WBV seems to improve inter- and intramuscular coordination in the neuromuscular system. Authors (Kerschau-Schindl et al., 2001; Rittweger et al., 2005) have reported that the application of vibrations increases bone formation and metabolism in skeletal muscles and skin. Rittweger et al, 2005 have suggested that WBV could prevent the loss of bone and muscle mass in immobilized adults.

Different tools were used to evaluate patients with OI (see Table 2), but the “Brief Assessment of Motor Function” (BAMF) was used in all the studies discussed in this revision. The importance of this type of evaluation, as reported by Cintas, et al, 2003, is due to, with a hierarchical series of 10-point ordinal scales is possible to have a rapid description of gross motor, fine motor, and oral motor performance of patients. Suskauer et al., 2003 have used this tool to evaluate the temperament and physical performance in children with OI. Smith et al., 2009 have used the BAMF to verify the sensory motor and functional skills of dizygotic twins.

It is important to consider that in all the papers presented in this review, the conclusions indicate the importance of the WBV to improve clinical condition of the patients with OI.

The current study has some scientific limitations that must be considered in the interpretation of the findings. Caution should be taken when generalizing the results due to the methodological variations concerning the biomechanical parameters or the variability of the protocols used. Even though the present review has reported the characteristics of the interventions, and seems to be a relationship between these parameters and changes in the important symptoms of the OI patients and considering that we fail to provide insights into the physiological stimulus for increasing these outcomes in this population, we recognize the limitation that our results may not represent a general dose–response relationship. Probably, if a meta-analysis would be conducted, more accurate conclusions could be drawn. Although the authors have tried to retrieve the articles involving WBV and OI with the selected keywords, it is not sure that all studies on this topic have been identified, including articles that were not published in English and articles published in journals that were not indexed in the databases searched. In addition, the limited number of publications with high methodological quality must also be considered and this fact could, of course, affect the

evidence of the findings. Therefore, although it is difficult, studies with a higher methodological quality and focusing specifically on certain types of population would be desirable. Further, the population included in these studies was heterogeneous (different ages and genders, and diseases) and results should be reviewed with caution.

## Conclusion

Despite the limitations, none of the studies reported side-effects and therefore it may be concluded that mechanical vibration would be a safe and suitable strategy in the management of OI patients. Although, a reduced number of papers were found, WBV exercise would be beneficial especially improving the mobility and the functional parameters in this population as a therapeutic tool. Nevertheless, methodological flaws and differences among protocols indicate the need of more research in this area.

## Competing Interests

The authors declare that there are not financial competing interests (political, personal, religious, ideological, academic, intellectual, commercial or any other) in relation to this manuscript.

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